

*Amendment and Reply*

U.S. Serial No. 09/127,624

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**Remarks**

This Reply is responsive to the Office Action dated February 23, 2001. Reconsideration of the subject application in light of the remarks and amendments presented herein is respectfully requested pursuant to 37 CFR §1.112.

First, claim 30 has been amended above to correct format and punctuation, as requested in the Office Action on page 2. Thus, the objection to claim 30 may now be withdrawn. No new matter has been added.

The Office Action asserts that the original parent application does not contain support for the amounts of growth factors recited in claim 30, and that claim 30 is only entitled therefore to the filing date of the present application as an effective filing date. Applicants respectfully note that support for the recited amounts of growth factors may be found in original claim 2 of the parent application. Moreover, U.S. Patent No. 6,156,569, which issued from the parent application, specifically recites the amounts recited in claim 30 of the present application in claim 2 of the '569 patent. Therefore, the parent application must have had support for the claimed amounts because otherwise, the Examiner would be challenging by implication the patentability of claims issued in a U.S. Patent. Thus, all the pending claims are entitled to the priority date of the parent application.

Claims 1, 4, 5, 7, 8 and 29-40 were rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabled for a method of culturing avian PGCs for at least 14 days in culture in media comprising LIF, bFGF, IGF and SCF in sufficient amounts, allegedly fails to provide enablement for culturing avian PGCs in media comprising "growth factors in amounts sufficient to maintain said PGCs for at least 14 days" as broadly as claimed. Essentially, the Examiner's bases for the rejection are that (1) the presence of LIF, bFGF, IGF and SCF is considered to be essential to maintain the PGCs in culture for at least 14 days and therefore must be included in claims 1, 4, 5, 7, 8, 31-35 and 37-40; and (2) claims 32 and 38 are not enabled because "the art at the time of filing did not teach feeder cells that produced growth factors in amounts sufficient to maintain PGCs for at least 14 days." Applicants respectfully traverse both grounds for the rejection.

Applicants respectfully submit that the presence of LIF, bFGF, IGF and SCF is only one combination of cofactors that will support the growth of avian PGCs in culture for at least

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14 days, and those of skill in the art could identify other combinations of cofactors in order to achieve the same result without undue experimentation, based on the knowledge provided by Applicants that such long term maintenance is made possible by use of the disclosed factors. Applicants were the first to achieve such long term maintenance of avian PGCs in culture as admitted by the Office in the previous Office Action. Indeed, as stated by the Office in the previous Action, the claims “are free of the prior art because the claims require that a pure population of PGCs be cultured for 14 days [and the] prior art did not teach or fairly suggest that PGCs could be cultured for this period of time without differentiating” (Paper No. 7, paragraph 12). Accordingly, Applicants are justifiably entitled to a claim of sufficient scope as to warrant their novel contribution to the field. Note that the previous Office Action did not state that the claims were free of the prior art for the reason that the prior art failed to teach the use of the specific four factors; rather, the Action emphasized the novel nature of the length of culture achieved by applicants, implying novelty lies notably in the length of the culturing achieved.

The Office has recognized such pioneering developments with claims of appropriate breadth in the past. For instance, in U.S. Patent 5,821,121 (‘121), claim 1 is broadly directed to a culturing method whereby human pancreatic cells are cultured for at least three months *in vitro*. Only in dependent claim 3 of the ‘121 patent do we see that the medium used for such culturing comprises:

- (i) a basal medium comprising essential minerals, salts, vitamins, amino acids, and lipids;
- (ii) a buffering system;
- (iii) glutamine in the amount of about 6.18 mM to about 8.36 mM;
- (iv) at least one energy source selected from the group consisting of lactate and pyruvate;
- (v) zinc in the amount of about 0.00446 mM to about 0.00604 mM;
- (vi) niacinamide in the amount of about 0.0264 mM to about 0.0358 mM, and
- (vii) myoInositol in the amount of about 0.271 mM to about 0.367 mM.

Likewise, in U.S. Patent No. 5,942,435, independent claim 1 is directed to a culturing method for isolating a swine embryo stem cell culture that requires only subculturing the culture until a stable culture with morphological features and growth parameters characteristic of an embryonic stem cell culture is established. Not until dependent claims 2 and 3 of the

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patent does the patentee assert that the medium for isolating the subculture of swine cells is conditioned by Buffalo Rat Liver Cells, growth factors, vitamins, amino acids and antibiotics, and that the medium more particularly comprises approximately 40% of stem cell medium (SCM) and approximately 60% of Buffalo Rat Liver Cell conditioned medium (BRL/CM). Thus, the Office has clearly been willing in the past to grant broad protection for culturing methods where applicants made important advances in culturing previously difficult-to-culture cells, and has awarded such applicants with claims that appropriate protect their pioneering advances.

The Federal Circuit stated the following in *In re Zletz*, 13 USPQ2d 1320, 1322 (1989) (with emphasis):

During patent examination the pending claims must be interpreted as broadly as their terms reasonably allow. When the applicant states the meaning that the claim terms are intended to have, the claims are examined with that meaning, in order to achieve a complete exploration of the applicant's invention and its relation to the prior art. See *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969) (before the application is granted, there is no reason to read into the claim the limitations of the specification). The reason is simply that during patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed. *Burlington Industries, Inc. v. Quigg*, 822 F.2d 1581, 1583, 3 USPQ2d 1436, 1438 (Fed. Cir. 1987); *In re Yamamoto*, 740 F.2d 1569, 1571, 222 USPQ 934, 936 (Fed. Cir. 1984). The issued claims are the measure of the protected right. *United Carbon Co. v. Binney & Smith Co.*, 317 U.S. 228, 232, 55 USPQ 381, 383-84 (1942) (citing *General Electric Co. v. Wabash Appliance Corp.*, 304 U.S. 364, 369, 37 USPQ 466, 468-69 (1938)).

Given the willingness of the Office to issue broad claims for pioneering culturing methods whereby applicant achieves long term culture of previously difficult-to-culture cells as illustrated by the patents discussed above, and given the position of the Federal Circuit that claims are to be examined as presented in order to establish their relation to the prior art, it is inappropriate to require the limitation of the specific growth factors to be read into the claims from the specification. Withdrawal of this ground for the rejection is respectfully requested.

As a second grounds for the rejection under §112, first paragraph, the Examiner indicated that claims 32 and 38 are allegedly not enabled "because the specification does not

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teach any feeder cells that provide growth factors in amounts sufficient to maintain PGCs for at least 14 days” (Office Action, page 5). Applicants respectfully submit that it is disclosed in the specification that feeder cells could be readily modified to express exogenous growth factors using techniques that are well known in the art. For instance, the specification discloses that “feeder cells may be transfected with genes encoding these growth factors, thereby eliminating the need for the exogenous addition of these factors during culturing . . . by placing these growth factor genes under control of constitutive promoter and also sequences that provide for the secretion thereof” (see page 13, lines 10-15). As such transfection and expression of exogenous genes was well within the skill of the art at the time the application was filed, and one of skill in the art could readily accomplish such transfection and expression absent undue experimentation, and given that applicant need not disclose that which is well known in the art, this ground for the rejection should be withdrawn. Reconsideration and withdrawal of the §112, first rejection in light of these remarks is respectfully requested.

Claims 1, 4, 5, 29-31, 33, 36, 37, 39 and 40 were rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 1-12 of U.S. Patent No. 6,156,569. Applicants respectfully request that this obvious-type double patenting rejection be held in abeyance until the indication of allowable subject matter, as the nature of the claimed subject matter may change during prosecution. If, at the indication of allowable subject matter the Examiner still believes such a rejection to be appropriate, applicants will consider filing a terminal disclaimer.

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This Reply is fully responsive to the Office Action dated February 23, 2001. Accordingly, a Notice of Allowance is next in order. If the Examiner has questions relating to the subject application or to this Reply, he is encouraged to contact the undersigned so that prosecution may be expedited.

Respectfully submitted,

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**APPENDIX: VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**In the Claims**

30. (Amended) The method of claim 29, wherein the minimum amounts of said growth [factor] factors are:

[40. 0.00625 U/ $\mu$ l LIF,]

- (i) 0.00625 U/ $\mu$ l LIF,
- (ii) 0.25 pg/ $\mu$ l bFGF,
- (iii) 0.5625 pg/ $\mu$ l SCF, and
- (iv) 4.0 pg/ $\mu$ l IGF.